Attorney Docket No. 5470-130DV

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Application of French et al.
Serial No.: 09/497,822
Filed: February 3, 2000

Group Art Unit: 1646
Examiner: M. Pak

For: ANDROGEN RECEPTOR PROTEINS, RECOMBINANT DNA MOLECULES CODING FOR SUCH, AND USE OF SUCH COMPOSITIONS

November 8, 2002

Commissioner for Patents
Washington, DC 20231

SUBMITTAL OF DECLARATION OF ELIZABETH M. WILSON, Ph.D PURSUANT TO 37 C.F.R. §1.132

Sir:

Attached for filing in the above-identified application is the Declaration of Elizabeth M. Wilson, Ph.D. Pursuant to 37 C.F.R. §1.132, including Appendices A-D.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, Washington, DC 20231, on November 8, 2002.

Susan E. Freedman

Susan E. Freedman
Date of Signature: November 8, 2002

ATTORNEY'S DOCKET NO. 5470-130DV

PATENT #19

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For: ANDROGEN RECEPTOR PROTEINS, RECOMBINANT DNA MOLECULES CODING FOR SUCH, AND USE OF SUCH COMPOSITIONS

Commissioner for Patents
Washington, DC 20231

Declaration of Elizabeth M. Wilson, Ph.D.

pursuant to 37 C.F.R § 1.132

I, Elizabeth M. Wilson, Ph.D., do hereby declare and say as follows:

1. I am a named inventor on U.S. Patent Application Serial No. 09/497,822 (*hereinafter* "the '822 application"). The work described in the '822 application was performed under the supervision and direction of me and my co-inventor Dr. Frank S. French.

2. The '822 application describes the cloning and sequencing of the rat androgen receptor. As presented in more detail in the '822 application, two rat clones, rat epididymis clones [1] and [2], were isolated from a rat epididymis cDNA library using as probes the complete human epididymis clone [1] and a EcoRl/Pstl fragment, cDNA probe [D], respectively. These rat clones contained the entire protein coding sequence for the rat androgen receptor. (See page 16, lines 25-29, of the above referenced application). Figure 6 of the '822 application presents the coding strand of the rat androgen receptor cDNA and the encoded primary amino acid sequence of the rat androgen receptor protein.

3. The cloning of the rat androgen receptor was described by Dr. French and myself in two publications:

- D.B. Lubahn et al., "Cloning of Human Androgen Receptor Complementary DNA and Localization to the X Chromosome", *Science* **240**:327-330 (published April 15, 1988).

- J.A. Tan et al., "The rat androgen receptor: primary structure, autoregulation of its messenger ribonucleic acid, and immunocytochemical localization of the receptor protein", *Mol. Endocrinology* **2**:1276-1285 (published December, 1988).

The sequences corresponding to the sequences of Figures 6 of the '822 application are published as Figure 2 of the Tan et al. (Mol. Endocrinology) paper. Reprints of these two papers are attached hereto at **Appendix A**.

4. The rat androgen receptor cDNA sequence was submitted to the Genome Sequence DataBase (GSDB) on August 18, 1988, and is available from GenBank (Accession number M20133). A copy of the GenBank report indicating the submission date of M20133 is attached hereto at **Appendix B**.

5. As noted in the Tan et al. paper, a positive clone (rARep1) was identified and plaque purified from a λgt11 rat epididymal cDNA library. After digestion with EcoRI, it was determined that clone rARep1 contained the sequence 5' to the DNA binding domain and that a second clone, rARep2, contained a 1.6 kbp insert and including the DNA-binding domain and the 3'-coding sequence. rARep1 and rARep2 are labeled rat epididymis clones [1] and [2] in the present application.

6. The cDNA clones rARep1 and rARep2 were then sequenced from the cloned restriction fragments diagrammed in Figure 1B of the Tan et al. article. The

composite sequence in Figure 2 illustrated the correct sequence of the rat androgen receptor.

7. It has recently come to my attention that the nucleotide and amino acid sequences of the rat androgen receptor shown in Figure 6 of the '822 application contain two errors as described in more detail below.

8. The first error involves the omission of one nucleotide that needs to be inserted after nucleotide 3805, and which results in an amino acid change. The second error involves the substitution of a "G" for a "C" at nucleotide 3812 (which will now be nucleotide 3813 after the insertion of a nucleotide at position 3806). (Applicants note that the incorrect nucleotides and amino acids are shown below as underlined and highlighted). Applicants also note that these errors change the reading frame.

Val Lys Pro Ile Tyr Phe His Thr Gln Stop correct sequence
GTC AAG CCC ATC TAT TTC CAC ACA CAG TGA AG
(starting nucleotide is #3802)

Val Ser Pro Cys Ile Ser Thr His Ser Glu Asp incorrect sequence
GTC AGC CCA TGT ATT TCC ACA CAC AGT GAA G

9. These errors were corrected after the filing of the '822 application (April 15, 1988), but before submission of the *Molecular Endocrinology* paper (received July 20, 1988 and accepted August 22, 1988) and before submission of the sequence to the Genome Sciences Database on August 18, 1988.

10. The sequencing of the λgt11 rARep1 and rARep2 clones was carried out by a graduate student, Mr. Jiann-an Tan, under the supervision and direction of myself and co-inventor Dr. Frank S. French. Mr. Tan independently read through the sequences on each strand of two independent λgt11 rARep1 and rARep2 clones. The sequence data were entered into a computer that compiled the information. If there were any discrepancies among the entered

sequences, they were resolved by re-examining the original films. If the disagreement persisted, the region in question was re-sequenced.

11. It appears likely that the sequencing errors described in Paragraph 8 above were the result of an incorrect reading or entry of data from the sequencing gels, and were routinely corrected by the verification procedure described in Paragraph 10.

12. Attached at **Appendix C** are protocols relating to the sequencing reactions encompassing the error described in Paragraph 8. These sequencing protocols were generated prior to April 15, 1988, the filing date of the '822 application. The protocols describe the analysis of a 0.7 kb EcoR1 fragment of the rat androgen receptor complementary DNA obtained from the larger approximately 1.6 kb EcoR1 fragment of the androgen receptor complementary DNA from a rat epididymis complementary DNA library. The 0.7 kb EcoR1 fragment was obtained from the 3' end of the 1.6 kb fragment due to an internal EcoR1 site. The 0.7 kb EcoR1 fragment was digested with the restriction enzyme Rsa1 to yield 2 fragments of approximately 300 bp and approximately 500 bp. The Rsa/R500 fragment contains the region that was misread.

13. Attached at **Appendix D** is a photograph of the film from sequencing gels of the region encompassing the error described in Paragraph 8. The sequencing protocols described above in Paragraph 12 and the accompanying film were generated prior to April 15, 1988, the filing date of the '822 application. The region of the picture that was misread is shown by a bracket that occurs just above the writing on the film that reads TGGCTCC. In viewing this region, one of skill in the art at this time would note that this region is compressed, thus, making an accurate reading difficult as compared to the region below this print. As indicated on the photograph, it can be seen that the correct sequence of GTC AAG CCC ATC TAT TTC CAC ACA CAG TGA was on the gel, but was either misread or misentered.

14. I have personally reviewed the original sequencing film described in Paragraph 13. It is clear from reviewing these films that the correct sequences of the λgt11 rARep1 and rARep2 clones described in Paragraph 8 were present on the sequencing gels (and the films), but that the sequencing information was initially mis-read or mis-entered into the computer. As described above, these errors in the sequence were corrected prior to the submissions to the Genome Sequence Database and *Molecular Endocrinology*.

16. I do hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 19 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Elizabeth M. Wilson, Ph.D. 10-31-02
Date

Attachments: Appendix A-D